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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,175	06/25/2004	Hirokazu Matsumoto	61536 (46342)	3286

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EXAMINER	
CHANDRA, GYAN	
ART UNIT	**PAPER NUMBER**
1646	

MAIL DATE	DELIVERY MODE
08/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,175	MATSUMOTO ET AL.	
	Examiner	Art Unit	
	Gyan Chandra	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *1-21 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22 and 24-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/25/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Re: Matsumoto et al.

Date of Priority: 12/28/2001 (403260)

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group VII (claims 22 and 24-38) and further election of the SEQ ID NO: 16 in the reply filed on 5/10/2007 is acknowledged. The traversal is on the ground(s) that the examination of additional sequences recited on page 82-97 would not be undue search burden. This is not found persuasive because the specification on pages 82-97, lists at least 149 different polypeptide sequences comprising SEQ ID NOs: 1, 2, 3, 3,.....148 and 149. Further, as explained on pages 3-4 of the previous office action of 4/11/2007, each of the claimed polypeptide sequences are composed of amino acid units and are structurally distinct molecules. Each sequence requires a unique separate search of the prior art. Searching for more than one claimed sequence would constitute an undue burden on the examiner and the USPTO's resource because of the non-coextensive nature of these searches. Therefore, additional sequences are distinct and separate inventions.

The requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, And/Or Claims

Claims 1-39 are pending.

Claims 1-21 and 23 are withdrawn from further consideration as being drawn to a nonelected Invention.

Claims 22 and 24-39 are under examination to the extent they read on the elected polypeptide of SEQ ID NO: 16.

Information Disclosure Statement

The Information Disclosure Statement filed on 06/25/2004 has been considered.

Claim Objections

Claims 22, 28, 29, 31, 32, 34, 35, 37 and 38 are objected for reciting non-elected inventions (i.e., SEQ ID NOs. 4, 6, 17, 20, 21...., and 149).

Claim 25 is objected for a typographical error for reciting SEQ ID NO: 26. The Examiner has interpreted "SEQ ID NO: 26" as "SEQ ID NO: 16".

The Examiner suggests the syntax of claim 22 can be improved by amending the claim as following:

(i) " which is characterized by administering....." to " wherein said method is characterized by administering....".

(ii) "in mammals" to "in a mammal"

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 22 and 24-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth a polypeptide of SEQ ID NO: 16 and therefore the written description is not commensurate in scope with any compound or any polypeptide which is substantially the same amino acid sequence as represented by SEQ ID NO: 16.

The claims broadly encompass any compound having an activity of the polypeptide of SEQ ID NO: 16 or any polypeptide variant of SEQ ID NO: 16 having substantially the same amino acid sequence as represented by SEQ ID NO: 16. However, the claims do not require that a compound possess any particular feature or structure that may exhibit any activity of the polypeptide of SEQ ID NO: 16.

The specification on pg.109, discloses that the polypeptide of SEQ ID NO: 16 is 23 amino acid residues in length and is possibly the human homolog of GPR8 ligand. The specification on pages 171-173, discloses that the polypeptide of SEQ ID NO: 16 (GPRL 1-23) when administered to rats, increases body weight. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. Some of the factual considerations that are weighed when determining a written description include the level of skill and knowledge in the art, the disclosure of complete or partial structures, the disclosure of physical and or chemical properties, adequate disclosure of the functional characteristics, the correlation between structure and function, and disclosure of methods of making.

In the instant case, the specification (on page 109, 171-173) only adequately discloses that the polypeptide of SEQ ID NO: 16 (GPR8L 1-23). The specification does not describe any compound that may include a nucleic acid, a fusion polypeptide, an antibody, or any small molecule that may have any activity of the polypeptide of SEQ ID NO: 16. Further, the specification does not describe any polypeptide which may be substantially the same amino acid sequence as represented by SEQ ID NO: 16 which may include any variant of the polypeptide of SEQ ID NO: 16. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is *whatever is now claimed* (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (see Vas-Cath at page 1116).

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly &

Co., 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In Regents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B (1), the court states an adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention.

As discussed above, the skilled artisan cannot envision the detailed genus of "compounds" or "any polypeptide having substantially the same amino acid sequence as represented by SEQ ID NO: 16", and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of making a mutation. The compound itself is required. See Fiers v.Revel, 25USPQ2d 1601 at 1606 (CAFC 1993) and Amgen v.Baird, 30 Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 148 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class.

Therefore, only a polypeptide comprising the amino acid sequence of SEQ ID NO: 16, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claims 22 and 24-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for increasing body weight in a mammal by administering a polypeptide of SEQ ID NO: 16 to said mammal, does not reasonably provide enablement a method of inhibiting body weight gain, adipose gain, promoting body weight loss, or feeding inhibition by administering (i) a polypeptide of SEQ ID NO: 16, (ii) any compound having any activity of the polypeptide of SEQ ID NO: 16 or (iii) a polypeptide having substantially the same amino acid sequence as represented by SEQ ID NO: 16. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable

one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986).

Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The instant disclosure fails to meet the enablement requirement for the following reasons:

Claims 22 and 24-39 are drawn to a method of inhibiting body weight gain, adipose gain, promoting body weight loss, or feeding inhibition in a mammal by administering (i) a polypeptide of SEQ ID NO: 16, (ii) any compound having any activity

of the polypeptide of SEQ ID NO: 16 or (iii) a polypeptide having substantially the same amino acid sequence as represented by SEQ ID NO: 16 to said mammal.

The state of the prior art and the predictability or lack thereof in the art:

Mori et al. (US Patent No. 7,193,033 published on 3/20/2007) teach a polypeptide of SEQ ID NO: 16 having 100% sequence identity to the instant polypeptide that stimulates appetite (see abstract, claim 1, and sequence alignment). Rohner-Jearnrenaud et al. (The New Eng. J. Med., 334: 324-325, 1996) teach that leptin is a hormone of adipocytes, and that the administration of leptin to ob/ob mice, reduces food intake and body weight (page 325, left column). Campfield et al (Science 280: 1383-1389, 1998) teach that the administration of leptin reduces food intake and body weight to lean mice, rats and monkey (page 1384, middle column). They teach that the administration of leptin to a subject provides multiple benefits such as appetite suppression, increase in metabolic rate and still reduces body fat. Grasso et al. (Endocrinol. 138: 1413-1418, 1997) teach that the C-terminus of the polypeptide leptin (amino acids 106-140) comprises leptin activities. The skill of the art for making an amino acid substitution or deletion is high. But, predicting function based on a change in a peptide is not predictable. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. As an example of the unpredictable effects of mutations on protein function, Mickle *et al* (Med. Clin. North Am., 2000, Vol. 84(3), p. 597-607) teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance

regulator (CFTR – p. 597). Several mutations can cause cystic fibrosis, including the G551D mutation. In this mutation, a glycine replaces the aspartic acid at position 551, giving rise to the cystic fibrosis phenotype. In the most common cystic fibrosis mutation, Δ-F508, a single phenylalanine is deleted at position 508, giving rise to the cystic fibrosis phenotype. Adelhorst et al (J. Biol. Chem. 269: 6275-6278, 1994) teach that a single mutation at position Phe28 (Phe22, re-numbered after truncation) to alanine results in a drastic reduction (~1300 fold) of GLP-1 binding to its receptor (see Table I, which is IC50 from 0.27nM to 351nM). Therefore, it would be unpredictable which compounds and variants of SEQ ID NO: 16 can be used to inhibit body weight gain, adipose gain, promoting body weight loss, or feeding inhibition in a mammal by administering (i) a polypeptide of SEQ ID NO: 16 to said mammal. Further, a large amount of experimentation would be required to make and use numerous compounds and variants of the polypeptide of SEQ ID NO: 16 which can inhibit body weight gain, adipose gain, promoting body weight loss, or feeding inhibition in a mammal that encompass the instant invention to enable the invention as broadly being claimed.

The amount of direction and guidance present and the presence or absence of working examples: Given the teachings found in the art, detailed teachings are required to be present in the disclosure in order to enable the skilled artisan to practice the invention as claimed. These teachings are absent. The specification on pages 171-173 discloses that the polypeptide of SEQ ID NO: 16 (GPR8L 1-23) when administered to a rat, stimulates body weight. The specification does not teach any example where administering the polypeptide of SEQ ID NO: 16, a polypeptide which is substantially

the same as represented by the SEQ ID NO: 16 or any compound having a activity of the polypeptide of SEQ ID NO: 16 can inhibit body weight gain or adipose tissue or promote body weight loss. Therefore, it is unpredictable how one of the skill in the art can practice the instantly claimed invention.

The breadth of the claims and the quantity of experimentation needed: Due to the large quantity of experimentation necessary to make and use numerous compounds having a activity of the polypeptide of SEQ ID NO: 16, or variants of the polypeptide of SEQ ID NO: 16 by administering to a mammal for inhibiting body weight gain or adipose tissue or promoting body weight loss, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability about administering any combination of the instantly claimed compounds or polypeptide variants that can inhibit body weight gain or adipose tissue or promote body weight loss in said mammal, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 22 and 24-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 22, the phrase "activity" renders the claim indefinite because it is not clear what activity the polypeptide or a compound has to have in order to meet the claim limitation. Therefore, the metes and bounds of the claim cannot be determined.

Claims 24-39 are rejected for directly or indirectly depending from an indefinite claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 22 and 24-39 are rejected under 35 U.S.C. 102(e) as being anticipated by Mori et al (US Patent No. 7,193,033 published on 3/20/2007 (US Pub No. 2005/0153391 A1) which claims benefit of PCT/JP01/05257 of 6/20/2001).

The applied reference has a common assignee, TAKEDA CHEMICAL INDUSTRIES, LTD, and common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the

reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

It is noted that the instantly claimed invention of inhibiting weight gain, adipose gain or promoting body weight is different from the teachings of Mori et al. But, Mori et al teach administering the same polypeptide as being claimed in the instant invention. Therefore, the reference Mori et al is being applied as a prior art.

Claims 22 and 24-39 are broadly drawn to a method of inhibiting body weight gain, adipose gain, promoting body weight loss, or feeding inhibition in a mammal by administering (i) a polypeptide of SEQ ID NO: 16, (ii) any compound having any activity of the polypeptide of SEQ ID NO: 16 or (iii) a polypeptide having substantially the same amino acid sequence as represented by SEQ ID NO: 16 to said mammal.

The instantly claimed method is achieved by administering an identical polypeptide (SEQ ID NO: 16) to a mammal, which is claimed in claim 6 of the reference Mori et al (see Sequence Alignment). Therefore, the outcome of administering an identical peptide would inherently be the same as claimed by Mori et al. Mori et al teach administering the polypeptide of SEQ ID NO: 16 in Wister male rats (see Example 24, column 79).

"Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)."

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RESULT 10
US-10-311-019B-16
; Sequence 16, Application US/10311019B
; Publication No. US20050153391A1
; GENERAL INFORMATION:
;  APPLICANT: MORI, Masaaki
;  APPLICANT:  SHIMOMURA, Yukio
;  APPLICANT:  HARADA, Mioko
;  APPLICANT:  ASAMI, Taiji
;  APPLICANT:  MATSUMOTO, Yoshio
;  APPLICANT:  ADACHI, Yuka
;  APPLICANT:  SUGO, Tsukasa
;  APPLICANT:  ABE, Michiko
;  APPLICANT:  GOTO, Mika nee KURIHARA
;  APPLICANT:  KITADA, Chieko
;  APPLICANT:  WATANABE, Takuya
;  TITLE OF INVENTION: Ligand for GPR8 and its DNA
;  FILE REFERENCE: 2739 USOP
;  CURRENT APPLICATION NUMBER: US/10/311,019B
;  CURRENT FILING DATE:  2002-12-11
;  PRIOR APPLICATION NUMBER: PCT/JP01/05257
;  PRIOR FILING DATE: 2001-06-20
;  PRIOR APPLICATION NUMBER: JP 2000-191089
;  PRIOR FILING DATE: 2000-06-21
;  PRIOR APPLICATION NUMBER: JP 2000-275013
;  PRIOR FILING DATE: 2000-09-06
;  PRIOR APPLICATION NUMBER: JP 2001-116000
;  PRIOR FILING DATE: 2001-04-13
;  NUMBER OF SEQ ID NOS: 125
; SEQ ID NO 16
;   LENGTH: 23
;   TYPE: PRT
;   ORGANISM: Human
US-10-311-019B-16

  Query Match             100.0%;  Score 127;  DB 5;  Length 23;
  Best Local Similarity   100.0%;  Pred. No. 7.4e-12;
  Matches   23;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 WYKHVASPRYHTVGRAAGLLMGL 23
              |||||||||||||||||||||||
Db          1 WYKHVASPRYHTVGRAAGLLMGL 23
```

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gyan Chandra whose telephone number is (571) 272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gyan Chandra
Art Unit 1646
02 July, 2007
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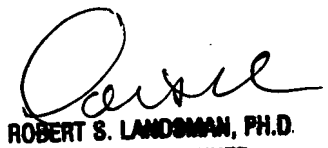

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